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FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary	Application No.	Applicant(s)	
	09/986,033	BUREAU ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-117* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. *9/341,350* .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

This application is a continuation of 09/341,350, filed July 9, 1999, now abandoned, which is a 371 National stage filing of PCT/FR98/01400, filed June 30, 1998, which claims benefit to US provisional application 60/067,488, filed December 1, 1997.

Applicants preliminary amendments both filed November 7, 2001, papers number 8 and 9, have been received and entered. The specification has been amended. Claims 1-84 have been canceled. Claims 85-117 have been added. Claims 85-117 are pending and currently under examination.

Election/Restriction

Applicant's election with traverse of Group IV, claims 109, 110 and 113, in Paper No. 12 is acknowledged. The traversal is on the ground(s) that it would not constitute a serious burden to examine all the inventions together. In particular Applicants note that all the inventions have the same classification. See Applicants' Election pages 2-3. This is found persuasive in part because upon review of the specification the inventive concept of the instantly claimed inventions is not the materials needed to practice the invention (i.e. specific nucleic acid sequences of angiogenic factors, hemostasis/blood-clotting factors, neurotrophic factors, and hematopoietic factors, and an eletroporation device) nor the outcome of practicing the methods by delivering specific factors (angiogenesis, hemostasis, nerve growth,...). Rather, the invention

relates to the observation that the cells of the muscle can be transfected by electroporation at relatively low voltages without undesirable effects created by using high voltages (specification bridging pages 5-6). The specification teaches that based on this observation accordingly, the invention is drawn to using electrical pulses of an intensity between 1 and 800 volts/cm^2 (page 6, lines 10-18). Because all the independent claims encompass the inventive aspect of the disclosed invention, that is electroporation of muscle cells *in vivo* with an electrical field intensity ranging from 1 to 800V/cm^2 , and the methods rely on the teachings in the art for the specific materials to practice the claimed methods, Examiner would agree that it would not constitute an undue burden to examine all the pending claims in light of the inventive concept of the claimed invention.

Therefore, the restriction requirement is withdrawn.

Specification

The disclosure is objected to because of the following informalities: applications cited in the priority claim should be updated to indicate the correct status of the application. In this case the specification should be amended to indicate that 09/341,350 has been abandoned.

Appropriate correction is required.

Oath/Declaration

It is noted that the parent application 09/341,350, filed July 9, 1999, was a National Stage filing of PCT/FR98/01400, filed June 30, 1998, however the declaration claims benefit to PCT/FR98/01400 under 35 U.S.C. 119 (see page 2). The claim for priority in the first line of the specification is inconsistent with that set forth in the declaration.

Clarification or correction is requested.

Information Disclosure Statement

A signed copy of the information disclosure filed February 11, 2002, paper number 3 has been included with the instant action.

Additionally, it is note that the listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." More specifically, the specification cites references that have not been listed in an IDS (for example at page 3, Manthorpe, 1993, Mumper, 1996) nor has a copy of the reference been provided. Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 90 and 93 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claim 90 recites that the "at least one striated muscle is a heart muscle cell" and claim 93 encompasses striated muscle segment in the heart, however the heart is composed of smooth muscle cells not striated muscle cells. The claim is unclear and confusing because the claim does not set forth embodiments that exist in nature.

Claims 92 and 94 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, claims 92 and 94 recite that the injection is "into a segment of striated muscle" however it is unclear what is considered a segment. This term is not defined in the specification nor is it conventional in the art. The claims are indefinite because the metes and bounds encompassed by a 'segment' are unclear.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 85, 103, 104 are rejected under 35 U.S.C. 102(a) as being anticipate by Dev *et al.* (WO 96/39226).

Dev *et al.* teach generally methods of delivering genes by using electroporation. Reviewing the prior art Dev *et al.* teaches that electroporation can be used to affect gene therapy (page 2, lines 25-30 and top of page 10). Dev *et al.* provide detailed guidance on the prior art and the specifications of devices known in the art. In particular, Dev *et al.* teach to use an electrical field of 100V/cm to several kV/cm (page 10, lines 20-25) and that the ECM 600 generator can provide 50-500 volts for LVM delivery (page 11, lines 5-10). Dev *et al.* teaches that the pulses can be set for various times and numbers of pulses (page 10, lines 10-15) and provides guidance for providing the optimum delivery with the minimum amount of peripheral damage to the cells (for example page 10, lines 3-9). Dev *et al.* teaches that electroporation can be used to deliver polynucleotides, in particular sequences which encode immunomodulatory agents (bridging pages 14-15) and which encode angiogenic compounds such as Factor IX (page 15, lines 7-8). Finally, Dev *et al.* teaches that the methods can be used for delivery to a variety of cells including the cells of the heart and muscle (page 16, lines 22-26). In summary, Dev *et al.* provide guidance

for the delivery of a polynucleotide to the cell of a muscle (a striated cell) and to use LVM ranges which anticipate the instant claims. The claims are anticipated by the teachings of Dev *et al.* because each of the limitations set forth in the claims are provided by Dev *et al.*

Claims 85, 103- 106 and 111 are rejected under 35 U.S.C. 102(e) as being anticipate by Dev *et al.* (US Patent 5,993,434).

Dev *et al.* '434 is similar to the disclosure of Dev *et al.* (WO 96/39226) set forth above. Reviewing the prior art Dev *et al.* teaches that electroporation can be used to affect gene therapy (columns 1-2). Dev *et al.* provide detailed guidance on the prior art and the specifications of devices known in the art. In particular, Dev *et al.* teach to use an electrical field of 100V/cm to several kV/cm (column 7, lines 15-20) and that the ECM 600 generator can provide 50-500 volts for LVM delivery (column 7, lines 38-47) and the T820 can be used to generate 100-300 volts at HVM setting and 50-500 boles at LVM setting (column 8, lines 5-10). Dev *et al.* teaches that the pulses can be set for various times and numbers of pulses (column 8, lines 5-10) and provides guidance for providing the optimum delivery with the minimum amount of peripheral damage to the cells (for example column 6, lines 58-67). Dev *et al.* teaches that electroporation can be used to deliver polynucleotides, in particular sequences which encode immunomodulatory agents and which encode angiogenic compounds such as Factor IX (column 10). Finally, Dev *et al.* teaches that the methods can be used for delivery to a variety of cells including the cells of the heart and muscle (column 11, lines 8-13). In summary, Dev *et al.* provide guidance for the delivery of a

polynucleotide to the cell of a muscle (a striated cell) and to use LVM ranges which anticipate the instant claims. The claims are anticipated by the teachings of Dev *et al.* because each of the limitations set forth in the claims are provided by Dev *et al.*

Claims 85, 103-106 and 111 are rejected under 35 U.S.C. 102(e) as being anticipate by Hofmann *et al.* (US Patent 6,241,701).

Reviewing the prior art Hofmann *et al.* teaches that electroporation can be used to affect gene therapy (columns 1-2). Hofmann *et al.* provide detailed guidance on the prior art and the specifications of devices known in the art. In particular, Hofmann *et al.* teach to use an electrical field of relatively low voltage being optimized for the tissue and apparatus being used. In particular Hofmann *et al.* teaches to use a range of 10V/cm to 20kV/cm for a variety of durations and a number of pulses. More specifically, Hofmann *et al.* teaches that optimum in vivo conditions are at 10V/cm to 1300V/cm where 600V/cm has been previously demonstrated to work. Moreover, Hofmann *et al.* teach that the optimum range will be with low fields of about 10V/cm to 100V/cm and preferably 25 V/cm to 75 V/cm (column 10, in particular lines 61-67). Hofmann *et al.* teaches that the pulses can be set for various times and numbers of pulses (column 15, lines 5-10) and provides guidance for providing the optimum delivery with the minimum amount of peripheral damage to the cells (for example bridging columns 14-15). Hofmann *et al.* teaches that electroporation can be used to deliver polynucleotides, in particular sequences which encode immunomodulatory agents and which encode angiogenic compounds

such as Factor IX (column 13, lines 46-64). Finally, Hofmann *et al.* teaches that the methods can be used for delivery to a variety of cells including the cells of the heart and muscle (column 14, lines 55-60). In summary, Hofmann *et al.* provide guidance for the delivery of a polynucleotide to the cell of a muscle (a striated cell) and to use LVM ranges which anticipate the instant claims. The claims are anticipated by the teachings of Hofmann *et al.* because each of the limitations set forth in the claims are provided by Hofmann *et al.*

Claim Rejections - 35 U.S.C. § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 85-117 are rejected under 35 U.S.C. 103(a) as being unpatentable over in view of Dev *et al.* (WO 96/39226 and '434) and Hofmann *et al.* (US Patent 6,241,701) in view of Wolff *et al.* (US Patent 5,693,622) and Wolff *et al.* (US Patent 56,228,844).

The anticipation of claim 85, 103-106 and 111 rejected under 35 U.S.C. 102 by Dev *et al.* (WO 96/39226 and '434) and Hofmann *et al.* (US Patent 6,241,701) is set forth above. Briefly, Dev *et al.* and Hofmann *et al.* provide guidance for the *in vivo* delivery of a polynucleotide to the cell of a muscle (a striated cell) and to use LVM ranges for the expression of angiogenic and hematopoietic factors in said cells to affect treatment in a subject. Both Dev *et al.* and Hofmann *et al.* teach that the methods of electroporation can be adapted to delivery any polynucleotide for treatment while specifically teaching the delivery of polynucleotide sequences that encode angiogenic and hematopoietic factors. However, Dev *et al.* and Hofmann *et al.* do not specifically set forth other the types of polynucleotide sequences useful in gene therapy treatments or the particular affects of expressing these sequences. At the time of filing Wolff *et al.* teach that gene therapy can be used for the delivery polynucleotide sequences encoding a variety of proteins useful for treatment. Both disclosures of Wolff *et al.* are similar teaching that the cells of the muscle are a preferable cell type ('622 column 10 lines 4-40 and column 16, lines 50-53). Further, Wolff *et al.* teach that a variety of methods known in the art can be used for delivery including electrorporation methodology ('622 column 16, lines 56-64). Finally, Wolff *et al.* teach that a variety of therapeutic proteins can be provided by gene therapy methods including the specific teaching for expressing growth hormones, GM-CSF, EPO ('622 column 15, lines 36-42) and VEGF ('844). Each Dev *et al.*, Hofmann *et al.* and Wolff *et al.* teach that a polynucleotide sequence encoding any gene of interest can be delivered to affect the necessary treatment in a subject. Each teach that delivery can be accomplished by electroporation

methodology *in vivo* to the cells of a tissue of interest including muscle, in particular Wolff *et al.* teach that the cells of the muscle are a preferred target cell. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the electroporation for the delivery of a polynucleotide in methods of gene therapy. Further, given the broad guidance of each for the expression of any gene of interest and the specific examples of therapeutic genes known in the art to be therapeutic other genes not specifically taught nor recited in Dev *et al.*, Hofmann *et al.* and Wolff *et al.* would be considered obvious gene of interest to the artisan because they would be considered obvious adaptations to affect specific affects in a subject. For example, at the time of filing it was well established that the presence of NGF was capable of stimulating nerve growth. One having ordinary skill in the art would have been motivated to combine the teachings of Dev *et al.*, Hofmann *et al.* and Wolff *et al.* because each specifically teach that electroporation can be used for the delivery of a gene of interest in gene therapy protocols. Further, each provide examples of and specific guidance for the expression of specific genes to affect specific affects in a subject. There would have been a reasonable expectation of success to effectively combine the teaching of Dev *et al.*, Hofmann *et al.* with that of Wolff *et al.* in light of the disclosure of the prior art for the successful use of electroporation *in vivo* and given the results of Wolff *et al.* for the ability to express a variety of genes of interest to affect treatment by gene therapy protocols

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Dev *et al.* US 202/0099323 provides further evidence for the successful use and desire to deliver to muscle cells by electroporation polynucleotide sequences encoding variety of therapeutic proteins.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Joseph T. Woitach

Joe Woitach

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